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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/902,692	07/30/1997	WILLIAM J. REA	16715CIP	1465
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EXAMINER SCHWADRON, RONALD B				
ART UNIT		PAPER NUMBER		
1644				
NOTIFICATION DATE		DELIVERY MODE		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

firm@ipoftexas.com
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Office Action Summary

Application No.

08/902,692

Applicant(s)

REA ET AL.

Examiner

Ron Schwadron, Ph.D.

Art Unit

1644

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 49-64, 67 and 70 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 49-64, 67, 70 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/CD/CS)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____
- Paper No(s)/Mail Date ____

1. Claims 49-64,67,70 are under consideration.
2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 49-64,67,70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants arguments have been considered and deemed not persuasive.

The specification is not enabling for the claimed method of treating a "chemical sensitive individual". Regarding Wands factors 4-8, the term "chemically sensitive individual" is not specifically defined in the specification. However, based on page 12, last paragraph, and page 15, last paragraph of the specification said patients apparently encompass those suffering from dermatitis, vasculitis, asthma, organic brain syndrome, gulf war syndrome or immune system specific suppression, dysfunction or deregulation and arthritis. However, Orme et al. indicates that it is unclear if a diagnostic entity such as the "chemically sensitive individual" (aka multiple chemical sensitivity) with the aforementioned diseases actually occurs (see page 6, third paragraph from the bottom). Orme et al. disclose that "Numerous scientific review bodies have concluded that there is no evidence to support the use of "multiple chemical sensitivity" as a diagnostic entity." (see page 6). Thus, it is unclear if the disease which the claimed invention treats exists as a clinical entity (see Orme et al., page 22). Orme et al. also indicate a high level of skepticism regarding the validity of treatments proposed for "multiple chemical sensitivity" (see pages 8-16). Barrett also reaches similar conclusions. Hall discloses that the connection between "chemical sensitivity" and the various diseases which the specification links to "chemical sensitivity" is questionable (see pages 1-4). In addition, regarding Inventor Rea and the use of the factor recited in the claims (aka ALF aka autogenous lymphocytic factor), Hall indicates that is unclear if

ALF can actually be used to treat disease (see pages 3-4). Barrett (2007) discloses a complaint filed against Inventor Rea filed with the Texas Medical Board which questions the validity of the diagnosis and treatment of chemical sensitivity as proffered by Inventor Rea. In addition, there is no evidence of record that indicates that "chemical sensitivity" causes vasculitis, organic brain syndrome, gulf war syndrome or immune system specific suppression, dysfunction or deregulation and arthritis.

The claimed invention encompasses the treatment of a wide variety of diseases "caused by chemical sensitivity" including patients suffering from dermatitis, vasculitis, asthma, organic brain syndrome, gulf war syndrome or immune system specific suppression, dysfunction or deregulation and arthritis. The aforementioned collection of diseases would encompass a plethora of autoimmune and inflammatory diseases. The specification discloses that said diseases involve chemical sensitivity and a dysfunctional cell cycle which is corrected by the treatment recited in the claims. However, as per above, the link between the aforementioned diseases and chemical sensitivity is unclear in view of the state of the art. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the use for the claimed methods is the in vivo treatment of a plethora of disease apparently linked to chemical sensitivity in humans. The state of the art is such that is unpredictable in the absence of appropriate evidence in humans as to whether the claimed invention can be used to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal wherein said method encompasses the in vivo treatment of humans to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes and the in vivo treatment of human disease.

Regarding the use of the claimed method to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal wherein said method encompasses the in vivo treatment of humans, there is no evidence in the specification that such regulation has been achieved using the claimed method. Regarding Wands factors 1-3, the claimed method encompasses a method wherein according to the specification the abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal is normalized. The only actual data disclosed in the specification wherein the cell cycle of human cells is analyzed is that

represented in Figures 2-4. Figures 2a and 2b represent data indicating the cell cycle of human peripheral T lymphocytes from "normal" volunteers. This data provides no information about the cell cycle of human peripheral B lymphocytes from "normal" volunteers. The specification indicates that abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal is regulated. Figures 3a -3c purport to show the "irregular cell cycle profiles from environmentally compromised individuals". There is no disclosure as to what cells are referred to in said figure (eg. only T cells, T and B cells, unfractionated lymphocytes, unfractionated leukocytes, etc.). Thus, it is unclear if there is any relationship between the data disclosed in Figure 2 and that in Figure 3 because it is unclear whether said Figures refer to the same or different cell populations. A similar problem exists with the data represented in Figure 4. Furthermore, if the data disclosed in Figure 4 refers to the cell cycle of T cells, it appears that the cell cycle of untreated patients in Figure 4a more closely approximates that seen in the normal controls than that seen in Figure 4c. Thus, the evidence of record suggests that the claimed method cannot be used to "regulate" the cell cycle of abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes because the term regulate would encompass normalization of an abnormal cell cycle and this has not been demonstrated. In addition, based on the data presented in the specification, it is unclear whether any effect on the cell cycle of continuously dividing B lymphocytes in a mammal has been achieved. Furthermore, regarding the data disclosed in Figure 4c, in the absence of appropriate control data (untreated patient) it is unclear whether the data presented represents a random fluctuation seen in patients unrelated to treatment. There is no evidence provided that the claimed invention can be used to regulate the abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in patients suffering from autoimmune disease. Thus, based on the disclosure in the specification, it is unclear as to whether the claimed invention can be used to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal wherein said method encompasses the in vivo treatment of a plethora of diseases in humans. Furthermore, the treated patients also received other treatments (for example see page 15) so it is unclear as to what treatments contributed to the "results" obtained in the specification in the absence of an appropriate control group. It is also noted that the number of cells used in the procedure disclosed in pages

9-10 to prepare ALF would yield a protein preparation with a concentration of any particular protein that would be far below that used for any biological modifier used to treat humans. For example, the use of rituximab in humans requires a dosage of approximately 750 mg per patient wherein said quantity requires billions to cells to produce such a quantity of molecule.

The specification does not disclose how to use the instant invention for the in vivo treatment of disease in humans. Applicant has not enabled the breadth of the claimed invention in view of the teachings of the specification because the use for the instant invention disclosed in the specification is the in vivo treatment of disease in humans. The state of the art is such that is unpredictable in the absence of appropriate evidence as to how the instant invention could be used for the in vivo treatment of disease in humans.

Judge Lourie stated in Enzo Biochem Inc. v. Calgene Inc. CAFC 52 USPQ2d 1129 that:

The statutory basis for the enablement requirement is found in Section 112, Para. 1, which provides in relevant part that:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same. . . . 35 U.S.C. Section 112, Para. 1 (1994). "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), which in this case is October 20, 1983 for both the '931 and '149 patents.

We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, e.g.,

Wands , 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands* , we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows:

(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Id. at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.* , 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

The *Wands* factors have been addressed above. It appears that undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification. See *In re Wands* 8 USPQ2d 1400(CAFC 1988).

Regarding applicants comments, the term "chemically sensitive individual" is not specifically defined in the specification. However, based on page 12, last paragraph, and page 15, last paragraph of the specification said patients apparently encompass those suffering from dermatitis, vasculitis, asthma, organic brain syndrome, gulf war syndrome or immune system specific suppression, dysfunction or deregulation and arthritis. The MPEP section 2111 [R-5] states:

2111 [R-5] Claim Interpretation; Broadest Reasonable Interpretation
CLAIMS MUST BE GIVEN THEIR BROADEST REASONABLE INTERPRETATION

During patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification." >The Federal Circuit's en banc decision in *Phillips v. AWH Corp.*, 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005) expressly recognized that the USPTO employs the "broadest reasonable

interpretation" standard: The Patent and Trademark Office ("PTO") determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction "in light of the specification as it would be interpreted by one of ordinary skill in the art." In re Am. Acad. of Sci. Tech. Ctr., 367 F.3d 1359, 1364[, 70 USPQ2d 1827] (Fed. Cir. 2004).

Thus, whilst the term "chemically sensitive individual" is not specifically defined in the specification, based on page 12, last paragraph, and page 15, last paragraph of the specification said patients apparently encompass those suffering from dermatitis, vasculitis, asthma, organic brain syndrome, gulf war syndrome or immune system specific suppression, dysfunction or deregulation and arthritis.

However, Orme et al. indicates that it is unclear if a diagnostic entity such as the "chemically sensitive individual" (aka multiple chemical sensitivity) with the aforementioned diseases actually occurs (see page 6, third paragraph from the bottom). Orme et al. disclose that "Numerous scientific review bodies have concluded that there is no evidence to support the use of "multiple chemical sensitivity" as a diagnostic entity." (see page 6). Thus, it is unclear if the disease which the claimed invention treats exists as a clinical entity (see Orme et al., page 22). Orme et al. also indicate a high level of skepticism regarding the validity of treatments proposed for "multiple chemical sensitivity" (see pages 8-16).

Hall discloses that the connection between "chemical sensitivity" and the various diseases which the specification links to "chemical sensitivity" is questionable (see pages 1-4). In addition, regarding Inventor Rea and the use of the factor recited in the claims (aka ALF aka autogenous lymphocytic factor), Hall indicates that it is unclear if ALF can actually be used to treat disease (see pages 3-4). *In addition, there is no evidence of record that indicates that "chemical sensitivity" causes vasculitis, organic brain syndrome, gulf war syndrome or immune system specific suppression, dysfunction or deregulation and arthritis.*

The claimed invention encompasses the treatment of a wide variety of diseases "caused by chemical sensitivity" including patients suffering from dermatitis, vasculitis, asthma, organic brain syndrome, gulf war syndrome or immune system specific suppression, dysfunction or deregulation and arthritis. The aforementioned collection of diseases would encompass a plethora of autoimmune and inflammatory diseases. The specification discloses that said diseases involve chemical sensitivity and a

dysfunctional cell cycle which is corrected by the treatment recited in the claims. However, as per above, the link between the aforementioned diseases and chemical sensitivity is unclear in view of the state of the art. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the use for the claimed methods is the in vivo treatment of a plethora of disease apparently linked to chemical sensitivity in humans. The state of the art is such that is unpredictable in the absence of appropriate evidence in humans to as to whether the claimed invention can be used to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal wherein said method encompasses the in vivo treatment of humans to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes and the in vivo treatment of human disease. The MPEP section 2164.03 [R-2] states:

2164.03 [R-2] Relationship of Predictability of the Art and the Enablement Requirement

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. >See, e.g., Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004)

Regarding the use of the claimed method to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal wherein said method encompasses the in vivo treatment of humans, there is no evidence in the specification that such regulation has been achieved using the claimed method. The specification states that chemical sensitivity is treated using the claimed method via regulating an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal.

Regarding Wands factors 1-3, the claimed method encompasses a method wherein according to the specification the abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal is normalized. The only actual data disclosed in the specification wherein the cell cycle of human cells is analyzed is that represented in Figures 2-4. Figures 2a and 2b represent data indicating the cell cycle of human peripheral T lymphocytes from "normal" volunteers. This data provides no information about the cell cycle of human peripheral B lymphocytes from "normal" volunteers. The specification indicates that abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal is regulated. Figures 3a -3c purport to show the "irregular cell cycle profiles from environmentally compromised individuals". There is no disclosure as to what cells are referred to in said figure (eg. only T cells, T and B cells, unfractionated lymphocytes, unfractionated leukocytes, etc.). Thus, it is unclear if there is any relationship between the data disclosed in Figure 2 and that in Figure 3 because it is unclear whether said Figures refer to the same or different cell populations. A similar problem exists with the data represented in Figure 4. Furthermore, if the data disclosed in Figure 4 refers to the cell cycle of T cells, it appears that the cell cycle of untreated patients in Figure 4a more closely approximates that seen in the normal controls than that seen in Figure 4c. Thus, the evidence of record suggests that the claimed method cannot be used to "regulate" the cell cycle of abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes because the term regulate would encompass normalization of an abnormal cell cycle and this has not been demonstrated. In addition, based on the data presented in the specification, it is unclear whether any effect on the cell cycle of continuously dividing B lymphocytes in a mammal has been achieved. Furthermore, regarding the data disclosed in Figure 4c, in the absence of appropriate control data (untreated patient) it is unclear whether the data presented represents a random fluctuation seen in patients unrelated to treatment. There is no evidence provided that the claimed invention can be used to regulate the abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in patients suffering from autoimmune disease. Thus, based on the disclosure in the specification, it is unclear as to whether the claimed invention can be used to regulate an abnormal lymphocytic cell cycle of continuously dividing T and B lymphocytes in a mammal wherein said method encompasses the in vivo treatment of a

plethora of diseases in humans.

Furthermore, the treated patients also received other treatments (for example see page 15) so it is unclear as to what treatments contributed to the "results" obtained in the specification in the absence of an appropriate control group. *It is also noted that the number of cells used in the procedure disclosed in pages 9-10 to prepare ALF would yield a protein preparation with a concentration of any particular protein that would be far below that used for any biological modifier used to treat humans. For example, the use of rituximab in humans requires a dosage of approximately 750 mg per patient wherein said quantity requires billions to cells to produce such a quantity of molecule.*

4. No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ron Schwadron/
Ron Schwadron, Ph.D.
Primary Examiner, Art Unit 1644

